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Novel alternating current electrospinning of hydroxypropylmethylcellulose acetate succinate (HPMCAS) nanofibers for dissolution enhancement: the importance of solution conductivity

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ABSTRACT

Novel high-yield alternating current electrospinning (ACES) as well as direct current (DCES) methods were investigated to prepare high quality hydroxypropylmethylcellulose acetate succinate (HPMCAS) fibers for the dissolution enhancement of poorly soluble spironolactone (SPIR). Although HPMCAS is of great pharmaceutical importance as a carrier of marketed solid dispersion-based products, it was found to be unprocessable using electrospinning. Addition of small amounts of polyethylene oxide as aid polymer provided smooth fibers with DCES but strongly beaded products with ACES. Solution characteristics were thus modified by introducing further excipients. In the presence of sodium dodecyl sulfate (SDS) high quality HPMCAS-based fibers were obtained even at higher throughput rates of ACES owing to the change in conductivity (rather than surface tension). Replacement of SDS to non-surface-active salts ($CaCl_2$ and NH_4Ac) maintained the fine quality of nanofibers confirming the importance of conductivity in ACES process. The HPMCAS-based fibers contained SPIR in an amorphous form according to DSC and XRPD. In vitro dissolution tests revealed fast drug release rates depending on the salt used to adjust conductivity. The presented results signify that ACES can be a prospective process for high scale production of fibrous solid dispersions in which conductivity of solution has a fundamental role.

Keywords based on the Journal's official list: dissolution, poorly water-soluble drugs, formulation, nanotechnology, oral drug delivery, excipients, polymeric drug delivery systems, solid dispersion

1. INTRODUCTION

Among the various types of cellulose derivatives, water-soluble compounds are key excipients in the practice of pharmaceutical formulation.[1] Sustained delivery of the drug is achievable through the slow gelation of non-ionic cellulose ethers such as hydroxypropylmethylcellulose (HPMC),[2] or if necessary, the disintegration of a tablet can be avoided in the stomach by applying anionic cellulose esters.[3] For instance, hydroxypropylmethylcellulose acetate succinate (HPMCAS) and hydroxypropylmethylcellulose phthalate (HPMCP) coatings are soluble only at the higher pH of the upper small intestine (i.e., above pH 5-5.5). Besides the application of cellulose ethers